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Appendix II (revised)

Table 1. Summary of scientific publications included in this New Dietary Ingredient notification reporting safety and effectiveness of Lyophilized *Saccharomyces Boulardii* (S.B.) in clinical trials. All of the S.B. used in these studies was manufactured and provided by Biocodex, Inc. (Reference numbers correspond to the bibliography in Appendix I)

Ref #	Study	Age of Subjects (yrs)	# of Subj.	Study Drug & Daily Dose (mg/day)	Efficacy	Safety
	Antibiotic-associated diarrhea					
1	McFarland, et al. *The Am. J. Gastroenterol.* (1995)	18 -86	193	Lyophilized S. B. 250 mg capsules (2 capsules, 2/day) **1000** mg /day	S.B. was effective in decreasing incidence of diarrhea: S.B. group: 7/97 (7.2%) Placebo: 14/96 (14.96%)	No significant adverse events were reported among patients receiving S.B.
2	Surawicz, et al. *Gastroenterol* (1989)	18 – 100	180	Lyophilized S. B. 250 mg capsules (2 capsules, 2/day) **1000** mg /day	S.B. was effective in decreasing incidence of diarrhea: S.B. group: 11/116 (9.5%) Placebo: 14/64 (21.8%)	No side effects were reported.
3	Adam, et al. *Médecine et Chirurgie Digestives* (1976)	≤ 16	388	Ultra-Levure® capsules (Lyophilized S. B.) 50 mg/capsules 4 capsules/day **200** mg/day	S.B. was effective in decreasing incidence of diarrhea: S.B. group: 9/199 (4.52%) Placebo: 33/189 (17.5%)	No side effects were reported.
	Clostridium difficile-associated diarrhea (CDD)					
4	McFarland, et al. *JAMA* (1994)	Adults	124	Lyophilized S. B. 250 mg capsules (2 capsules, 2/day) **1000** mg /day	S.B. was effective in decreasing incidence of recurrence of CDD: S.B. group: 26.3% recurrence Placebo: 44.8% recurrence	Thirst (n = 5) Constipation (n = 8)
5	Buts, et al. *J. Ped.*	0.2 - 11	19	Lyophilized S. B. < 1 yr: **500** mg/day	S.B. eliminated diarrhea in 18/19 (95%) of subjects.	No side effects were reported.

Ref #	Study	Age of Subjects (yrs)	# of Subjects	Study Drug & Daily Dose (mg/day)	Efficacy	Safety
	Gastroenterol. (1993)			1-4 yr: **750** mg/day > 4 yr: **1000** mg/day		
	Acute diarrhea					
6	Hecker, *Kinder- und Jugendmedizin* (2001)	0 – 17	940	Perenterol® (Lyophilized S. B.) 50-1500 mg/day 54.4% ≥ **500** mg/day 14.5% < 250 mg/day	Physicians' assessments: Efficacy: "very good" = 52%; "good" = 38% Tolerability: "very good" = 70%; "good" = 29%	1.7% experienced side effects (flatulence or allergic reactions). "The safety of using Perenterol [*S. boulardii*] even in small children, which had already been empirically shown during many years of extensive use …, was confirmed during the present study ***."
7	Hoechter, et al., *Munch. Med. Wschr.* (1990)	18-65	92	Perenterol® capsules (Lyophilized S. B.) 50 mg/capsule Days 1-2: **600** mg/day Days 3-7: 300 mg/day	S.B. significantly decreased frequency of loose stools within 2 days: S.B. group: 17.2% reduction Placebo: 13.6% reduction	"No severe side effects were observed in any patient." One patient in each group (S.B. and placebo) reported constipation or vomiting.
8	Chapoy, et al. *Annal. de Ped.* (1985)	Infants	38	Lyophilized S. B. 500 mg/sachet 1 sachet/day = **500** mg/day	S.B. significantly decreased the frequency and weight of loose stools.	"No side effects were noted and the acceptability of treatment was excellent."
9	Cetina-Sauri and S. Basto, *Trib. Med.* (1989)	0.25 - 3	130	Floratil® sachets (Lyophilized S. B.) 200 mg/sachet	S.B. significantly decreased the number of loose stools within 1 – 4 days.	"The number of clinical cures was larger than in the placebo group … there

Ref #	Study	Age of Subjects (years)	# in Study	Strain/Dosage Form/Daily Dose (mg/day)	Efficacy	Safety
				200 mg/8 hrs = **800** mg/day		were no side effects."
	Tube-fed patients					
10	Bleichner, et al., *Int. Care Med.* (1997) Multi-center, randomized, double blind, placebo controlled study.	≤ 18	128	Lyophilized S. B. sachets 500 mg/sachet 4 sachets/day = **2000** mg/day	S.B. significantly reduced the percentage of days with diarrhea: S.B. group: 14.2% Placebo: 18.9%	"The tolerance of *S boulardii* was good and no adverse effect was noted."
	AIDS					
11	Saint-Marc, et al. *Semaine des Hôpitaux* (1995) Randomized, double blind, placebo controlled study.	≥ 18	36	Lyophilized S. B. sachets 500 mg/sachet 6 sachets/day = **3000** mg/day (administered orally or via gastric tube)	A significantly higher percentage of subjects receiving S.B had diarrhea resolved within 1 week: S.B. group: 61% resolved Placebo: 12% resolved	"Tolerability was outstanding." "[T]olerability of *S. boulardii* was excellent in all patients, with a total absence of adverse effects …." "No clinical or paraclinical adverse events have occurred in the patients followed for a longer time."
	Traveler's Diarrhea					
12	Kollaritsch, et al., *Fortschr. Med.* (1993) Randomized, double	> 6	1016	Perenterol Forte® (Lyophilized S. B.) 250 mg/sachet 250-1000 mg /day	S.B. reduced the rate of diarrhea: S.B. group (n = 655): 28.7% Placebo (n = 361): 39.1%	"No severe side effects or disorders necessitating discontinuation of administration were

Ref #	Study	Age of Subjects (yrs)	# of Subj.	Study Drug & Daily Dose (mg/day)	Efficacy	Safety
	blind, placebo controlled study.			46 % of subjects in treatment group received **1000** mg/day	S.B. group: 303 (46%): 1000 mg/day 352 (54%): 250 mg/day	reported. This may demonstrate that the safety profile of SB is excellent and thus represents a more or less ideal prophylactic agent."